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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,532	03/12/2007	Moon-Hi Han	95981	3551

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/566,532	Applicant(s) HAN ET AL.	
	Examiner ANN Y. LAM	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _05 November 2008_.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1-7_ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _5-7_ is/are allowed.

6)☒ Claim(s) _1 and 2_ is/are rejected.

7)☒ Claim(s) _3 and 4_ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _11/7/08_.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kling et al., 7105508, in view of Kumar et al., 6218136, and further in view of Grace et al., 6,801,677.

As to claims 1 and 2, Kling et al. teach that integrin alpha..sub.v.beta..sub.3 antagonists were identified and assessed by using an assay system based on competition between the natural integrin .alpha..sub.v.beta..sub.3 ligand vitronectin and the test substance for binding to solid phase-bound integrin .alpha..sub.v.beta..sub.3. Microtiter plates were coated with integrin .alpha..sub.v.beta and contacted with vitronectin and anti-human vitronectin antibody coupled to peroxidase, washed with an assay buffer, and then peroxidase substrate was added and adbsorption was measured. Concentration of the antagonist at which 50% of the ligand is displaced (col. 105, line 53 – col. 106, line 8.)

However, Kling et al. teach using peroxidase as the label rather than a fluorescent label.

Kumar et al. however teach that there are many ways to configure an assay to look for compounds which inhibit the binding of, in this particular case, MAPKAP kinase-3 to CSBP. Kumar et al. disclose that a common screening format uses a 96-well plate in which MAPKAP kinase-3 is initially attached to the wells of an ELISA plate. Subsequently a solution containing the putative inhibitor is added mixed with a solution containing CSBP. The bound CSBP in each well is then measured. Kumar et al. disclose that this is typically done by labeling the CSBP with a fluorescent label which can be detected directly, or by incubating with an additional reagent which detects the bound CSBP, such as an antibody specific for CSBP which has been fluorescently tagged or conjugated to an enzyme such as horseradish peroxidase, whose presence can be measured through an enzymatic reaction by providing a substrate which results in a color change. Kumar et al teach that these and other variations to ELISA plate assays are well known to those in the art. Typically, the amount of protein used in each step and the exact combination of reagents are determined empirically. Antagonist or inhibitor compounds which block the interaction of MAPKAP kinase-3 with CSBP are those which lead to a reduced signal. The assay can also be configured with the CSBP attached to the well, and the MAPKAP kinase-3 is added with candidate inhibitor compound as the second step followed by detection reagents as described above for CSBP. (col. 9, lines 12-49.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a fluorescent label as a substitute for the horseradish peroxidase label in the Kling et al. invention since this is a simple substitution of one

known equivalent for another, as disclosed by Kumar et al. Utilizing a chip is within the skills of the ordinary artisan as chips are known in the art for performing assays, as exemplified by Kumar et al.'s disclosure of another assay format using a chip (see col. 9, lines 59-63). As to a step of washing the chip with buffer solution after reacting and before measuring the degree of ligand binding, such washing step is typical in the art to remove non-bound or non-reacted materials including non-bound labeled materials in order to detect only those that are bound. Such a washing step is also exemplified by Kumar et al. as shown above (although using the peroxidase labeling technique.) The skilled artisan would recognize that such washing is necessary in a direct fluorescent assay to measure the degree of binding, as indicated by the detection of the bound fluorescent label.

Also, neither Kling et al. nor Kumar et al. teach that the protein chip is coated with a monolayer of a bifunctional linking means.

However, Grace et al. disclose that calixarenes can be functionalized to permit attachment to a waveguide surface and can optimize binding to selected analytes. (col. 8, lines 33-37.) It is also disclosed that calixarene derivatives with substituents in the para position have deeper, larger cavities and thereby permit more control of binding to target analytes (col. 8, lines 44-46.) (The calixarene is a bifunctional linker since it links to the solid support on one side and to a molecule on another side.)

While Grace et al. disclose that calixarene derivatives can be used to bind target analytes to a waveguide surface, the skilled artisan would have recognized that binding chemistries used for immobilizing target analytes are also used for immobilizing

molecules that are not themselves analytes but are probes for the analytes. Thus it would have been obvious to the skilled artisan that calixarene derivatives can be used to bind integrin alpha..sub.v.beta..sub.3, to a substrate, such as the substrate (chip) disclosed by Kling et al. Moreover the skilled artisan would have reasonable expectation of success in using calixarene derivatives to bind integrin alpha..sub.v.beta..sub.3, since Grace et al. teach that calixarene can be functionalized as required for permitting binding of a specific molecule, and that calixarene derivatives can have deeper, larger cavities, permitting more control of binding to molecules. Moreover,it would have been within the skills of the ordinary artisan to provide the calixarene as a coating on the solid support in order to immobilize the molecules to the solid support. Such a coating is equivalent to a monolayer.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kling et al., 7105508, in view of Kumar et al., 6218136, and further in view of Chiu et al., 6,986,992.

As to claims 1 and 2, Kling et al. teach that integrin alpha..sub.v.beta..sub.3 antagonists were identified and assessed by using an assay system based on competition between the natural integrin .alpha..sub.v.beta..sub.3 ligand vitronectin and the test substance for binding to solid phase-bound integrin .alpha..sub.v.beta..sub.3. Microtiter plates were coated with integrin .alpha..sub.v.beta and contacted with vitronectin and anti-human vitronectin antibody coupled to peroxidase, washed with an

assay buffer, and then peroxidase substrate was added and adbsorption was measured. Concentration of the antagonist at which 50% of the ligand is displaced (col. 105, line 53 – col. 106, line 8.)

However, Kling et al. teach using peroxidase as the label rather than a fluorescent label.

Kumar et al. however teach that there are many ways to configure an assay to look for compounds which inhibit the binding of, in this particular case, MAPKAP kinase-3 to CSBP. Kumar et al. disclose that a common screening format uses a 96-well plate in which MAPKAP kinase-3 is initially attached to the wells of an ELISA plate. Subsequently a solution containing the putative inhibitor is added mixed with a solution containing CSBP. The bound CSBP in each well is then measured. Kumar et al. disclose that this is typically done by labeling the CSBP with a fluorescent label which can be detected directly, or by incubating with an additional reagent which detects the bound CSBP, such as an antibody specific for CSBP which has been fluorescently tagged or conjugated to an enzyme such as horseradish peroxidase, whose presence can be measured through an enzymatic reaction by providing a substrate which results in a color change. Kumar et al teach that these and other variations to ELISA plate assays are well known to those in the art. Typically, the amount of protein used in each step and the exact combination of reagents are determined empirically. Antagonist or inhibitor compounds which block the interaction of MAPKAP kinase-3 with CSBP are those which lead to a reduced signal. The assay can also be configured with the CSBP attached to the well, and the MAPKAP kinase-3 is added

with candidate inhibitor compound as the second step followed by detection reagents as described above for CSBP. (col. 9, lines 12-49.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a fluorescent label as a substitute for the horseradish peroxidase label in the Kling et al. invention since this is a simple substitution of one known equivalent for another, as disclosed by Kumar et al. Utilizing a chip is within the skills of the ordinary artisan as chips are known in the art for performing assays, as exemplified by Kumar et al.'s disclosure of another assay format using a chip (see col. 9, lines 59-63). As to a step of washing the chip with buffer solution after reacting and before measuring the degree of ligand binding, such washing step is typical in the art to remove non-bound or non-reacted materials including non-bound labeled materials in order to detect only those that are bound. Such a washing step is also exemplified by Kumar et al. as shown above (although using the peroxidase labeling technique.) The skilled artisan would recognize that such washing is necessary in a direct fluorescent assay to measure the degree of binding, as indicated by the detection of the bound fluorescent label.

Morever, neither Kling et al. nor Kumar et al. disclose use of a bifunctional linking means. However, Chiu et al. teach that the method of attachment of the capture probe to the detection surface can be done in a variety of ways, depending on the composition of the "capture binding ligand" or "capture probe" and the composition of the detection surface. Both direct attachment or indirect attachment can be used. Indirect attachment is done using an attachment linker. In general, both ways utilize

functional groups on the capture probe, the attachment linker or spacer, and the detection surface for covalent attachment. Preferred functional groups for attachment are amino groups, carboxy groups, oxo groups and thiol groups. These functional groups can then be attached, either directly or indirectly through the use of a linker, sometimes depicted herein as "Z". "Linkers" or "spacers" or "anchoring groups" are well known in the art; for example, homo- or hetero-bifunctional linkers as are well known. Preferred modifications useful in the practice of the invention include, but are not limited to, --OH, --NH.sub.2, --SH, --COOR (where R.dbd.H, lower (C.sub.1-12) alkyl, aryl, heterocyclic alkyl or aryl, or a metal ion), --CN, or --CHO. Immobilization of such derivatized probes is accomplished by direct attaching of the probe molecules on the detection surface through a functional group such --OH, --SH, --NH.sub.2. Column 29, line 66 to column 30, line 31.

It would have been obvious to the skilled artisan to utilize known means for attaching the probes of Kling et al. and thus use of bifunctional linkers, as well known in the art as disclosed by Chiu et al. is within the skills of the ordinary artisan.

Allowable Subject Matter

Claims 3 and 4 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 5-7 are allowed.

The following is a statement of reasons for the indication of allowable subject matter. The peptides recited in claim 3 is interpreted to mean the peptide **consists of** SEQ ID NO:1, or SEQ ID NO:2, etc. The prior art does not disclose such peptides nor its use.

Response to Arguments

Applicant's arguments with respect to claims 1 and 2 have been considered.

Applicant has amended the claims to replace calixarene with a monolayer of a bifunctional linking means. Applicant argues that in using the monolayer of bifunctional linking means, the cavity of the calixarene is not used but rather the lower part of the monolayer of a bifunctional moleuclar linking means is substituted by the crown ring and the crown ring detects the target of substances or molecules. Examiner notes however that this is not claimed. The calixarene is inherenlty a bifunctional linker since it links to the solid support on one side and to the molecule/probe on the other side. A coating of the calixarene, as would be obvious in immobilizing a probe, is equivalent to a monolayer.

Applicant’s arguments regarding a chip and microtiter plate are persuasive and the grounds for rejection have been amended accordingly.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641